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— *of inventorship (Rule 4.17(iv)) for US only*

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*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: NEUROPILIN-1 INHIBITORS

(57) Abstract: The present invention relates to molecules interfering with the function of neuropilin-1 in the context of angiogenesis and the treatment of cancer. Molecules, polypeptides, antibodies, compositions and methods are provided that are useful for reducing, inhibiting or treating angiogenesis, the invasion of blood vessels into tumors, and/or the invasion or the metastatic potential of specific tumor cells. Additionally, a method is provided that allows identifying molecules, which interfere with the functionality of neuropilin-1. Furthermore, a method is provided that allows determining whether a naturally occurring tumor cell depends on functional neuropilin-1 for its invasiveness and/or metastatic potential.

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## INTERNATIONAL SEARCH REPORT

International Application No

T/EP 03/14756

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/30 C07K16/28 A61K39/395 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, MEDLINE, BIOSIS, EMBASE, WPI Data, PAJ, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 99/55855 A (LEE YOON S ;WRIGHT JIM A (CA); YOUNG AIPING H (CA); GENESENSE TECH) 4 November 1999 (1999-11-04) examples page 2, lines 10-12 page 6, lines 13-22</p> <p style="text-align: center;">-/-</p>	1-22

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

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COVONE-VAN HEES, M

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/14756

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 7,8,21,22 (partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 8,21,22 are directed to a method of treatment of the human/animal body, and claim 7 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/14756

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9955855	A	04-11-1999	AU 749802 B2	04-07-2002
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			WO 02086157 A2	31-10-2002
			US 2004152110 A1	05-08-2004

## INTERNATIONAL SEARCH REPORT

International Application No

T/EP 03/14756

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ROCHE JOELLE ET AL: "Semaphorin SEMA3F inhibits cell attachment and spreading in human mammary tumor cells"</p> <p>PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 43, March 2002 (2002-03), pages 22-23, XP001182920</p> <p>&amp; 93RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; SAN FRANCISCO, CALIFORNIA, USA; APRIL 06-10, 2002</p> <p>ISSN: 0197-016X</p> <p>abstract</p>	1,8,10, 14,15, 21,22
X	<p>TAKAHASHI TAKUYA ET AL: "Semaphorins A and E act as antagonists of neuropilin-1 and agonists of neuropilin-2 receptors"</p> <p>NATURE NEUROSCIENCE, vol. 1, no. 6, October 1998 (1998-10), pages 487-493, XP002295428</p> <p>ISSN: 1097-6256</p> <p>abstract</p> <p>page 487, left-hand column, lines 16-19</p> <p>page 492, left-hand column, paragraph 1</p> <p>figure 1</p>	1,6-8, 10-12
X	<p>MATTHIES ANNETTE M ET AL: "Neuropilin-1 participates in wound angiogenesis"</p> <p>AMERICAN JOURNAL OF PATHOLOGY, vol. 160, no. 1, January 2002 (2002-01), pages 289-296, XP002295429</p> <p>ISSN: 0002-9440</p> <p>page 290, left-hand column, paragraph 2</p> <p>page 291, left-hand column, paragraph 3 - right-hand column, paragraph 1</p> <p>page 292, left-hand column</p> <p>figure 3</p> <p>page 295, left-hand column, last paragraph</p>	1,7-10
X	<p>HIDEYASU OH ET AL: "Selective induction of neuropilin-1 by vascular endothelial growth factor (VEGF): a mechanism contributing to VEGF-induced angiogenesis"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 1, 8 January 2002 (2002-01-08), pages 383-388, XP002255027</p> <p>ISSN: 0027-8424</p> <p>page 387, left-hand column, paragraph 2 - right-hand column, paragraph 1</p> <p>figure 3</p> <p>Discussion</p>	1,7,8, 10,13

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## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/086157 A (ALGARTE-GENIN MICHELE ;LATIL ALAIN (FR); UROGENE SA (FR); CUSSENOT) 31 October 2002 (2002-10-31)  page 5, lines 18-31 page 11, lines 17-34 page 21, line 1 - page 22, line 26	1,8, 10-12, 14-16, 21,22
A		4
A	JAY D G: "SELECTIVE DESTRUCTION OF PROTEIN FUNCTION BY CHROMOPHORE-ASSISTED LASER INACTIVATION" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 85, no. 15, August 1988 (1988-08), pages 5454-5458, XP000857275 ISSN: 0027-8424 the whole document	6